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Clean Version of Pending Claims

GENETIC MODIFICATION OF ENDOSTATIN
Applicant: Yumi Yokoyama et al.
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1. A composition comprising: a chimeric polypeptide comprising a peptide or polypeptide targeting moiety specific for endothelial cells linked to an antiangiogenic polypeptide.

2. The composition of claim 1 wherein the targeting moiety binds to integrin on endothelial cells.

3. (Amended) The composition of claim 2 wherein the targeting moiety comprises RGD, NGR, RGDNGR (SEQ ID NO:8), or NGRRGD (SEQ ID NO:9).

4. The composition of claim 2 wherein the targeting moiety binds to $\alpha_v\beta_3/\alpha_v\beta_5$ integrins.

5. The composition of claim 1 wherein the targeting moiety and the anti-angiogenic polypeptide are linked via a peptide bond.

6. The composition of claim 1 wherein the targeting moiety is linked to the amino terminus of the anti-angiogenic polypeptide.

7. The composition of claim 1 wherein the targeting moiety is linked to the carboxy terminus of the antiangiogenic polypeptide.

8. The composition of claim 1 wherein the antiangiogenic polypeptide is endostatin.

9. The composition of claim 8 wherein the amino acid at position 125 in endostatin is not proline.

10. The composition of claim 9 wherein the amino acid at position 125 is alanine, valine, leucine, isoleucine or methionine.

11. The composition of claim 1 wherein the antiangiogenic polypeptide is angiostatin.

12. The composition of claim 1 wherein the antiangiostatic polypeptide is kringle 5 of plasminogen, angiostatin (kringle 1-4 of plasminogen), tumstatin, canstatin, anti-thrombin fragment or retinal pigment derived factor.

13. The composition of claim 1 further comprising a pharmaceutically acceptable diluent.

14. The composition of claim 8 wherein the targeting moiety is RGD.

15. A sustained release dosage form comprising the composition of claim 1.

16. The sustained release dosage form of claim 15 which comprises alginate beads.

17. A host cell transformed with recombinant DNA encoding a chimeric polypeptide comprising a peptide or polypeptide targeting moiety specific for endothelial cells linked to an antiangiogenic polypeptide.

18. A method to inhibit or prevent undesirable endothelial cell proliferation or migration, comprising: contacting a mammalian endothelial cell with an amount of the composition of claim 1 effective to inhibit or prevent undesirable endothelial cell proliferation or migration.

19. The method of claim 18 wherein the mammalian cell is a human cell.

20. The method of claim 18 wherein the composition comprises a RGD-containing peptide linked to endostatin.

21. A therapeutic method comprising: administering to a mammal having a condition characterized by undesirable endothelial cell proliferation or migration, a dosage from comprising an effective amount of the composition of claim 1.

22. The method of claim 21 wherein the condition is cancer, diabetic retinopathy, macular degeneration, or restenosis.

23. The method of claim 21 wherein the condition is colon cancer.

24. The method of claim 21 wherein the condition is ovarian cancer.

25. The method of claim 21 wherein the dosage form is a sustained release dosage form.

26. The method of claim 25 wherein the sustained release dosage form comprises alginate.

27. The method of claim 18 or 21 wherein the antiangiogenic polypeptide in the composition is kringle 5 of plasminogen, angiostatin (kringle 1-4 of plasminogen), tumstatin, canstatin, anti-thrombin fragment or retinal pigment derived factor.

28. The method of claim 18 or 21 wherein the antiangiostatic polypeptide in the composition is endostatin.

29. The method of claim 28 wherein amino acid at position 125 of endostatin is not a proline.

30. The method of claim 29 wherein the amino acid at position 125 is alanine, valine, leucine, isoleucine or methionine.

31. (Amended) The method of claim 18 or 21 wherein the targeting moiety is RGD, NGR, RGDNGR (SEQ ID NO:8), or NGRRGD (SEQ ID NO:9).

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